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WOLF, BLOCK, SHORR AND SOLIS-COHEN LLP
250 PARK AVENUE
10TH FLOOR
NEW YORK, NY 10177

EXAMINER	
BEISNER, WILLIAM H	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,761	HUNG ET AL.	
	Examiner	Art Unit	
	William H. Beisner	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. Applicant is advised that should claim 38 be found allowable, claim 75 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-28, 30, 36, 37, 61, 62, 64, 65, 67-69, 72-74, 76-78, 81 and 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. All of the above claims include the new claim limitation of a "means for controlling the strain-controlled deformational loading according to a loading regime for producing functional cartilaginous tissue". As evident from the instant claim language, this appears to be a structure that is different from the structure or means for applying the load. After review of the originally filed disclosure, it is not readily

apparent to the Examiner where support can be found for this claim language and/or what corresponding structure is disclosed in the specification that will perform the recited function. Note Applicants' response fails to indicate where support for this means plus function language can be found and/or what structures in the originally filed specification would correspond to this newly recited means.

4. Claims 1-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite a bioreactor and method of using to produce a "functional cartilaginous tissue". While the specification provides some guidance with respect to the specific device employed for holding and applying the loads to the cells and wide ranges of strain, hydrostatic pressure, frequency, time applied and length of time cultured, the specification indicates that the applied strain and hydrostatic pressure are "critical" and are "optimized" for achieving the desired functional tissue (See page 16, line 8, to page 17, line 28). While the specification provides a wide ranges of strain, hydrostatic pressure, frequency, time applied and length of time cultured, no working examples and/or quantifiable evidence are provided to convey to one of ordinary skill in the art what optimal conditions would produce a functional cartilaginous tissue as required of the instant claims. Page 13 of the instant specification evidences that the culturing of cartilage tissue to produce functional cartilage is unpredictable since functional cartilage is desired but not always obtained. Without the missing disclosure and in view of the

unpredictability in the art, one skilled in the art would not know which combination of strain, hydrostatic pressure, frequency, and/or length of time would result in a tissue as required in the instant claims and, accordingly, one skilled in the art would be required to perform undue experimentation to optimize the loading regime for producing functional cartilaginous tissue. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 13-19, 22-35, 58-61, 65, 66, 68, 70, 77, 79 and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al.(WO 98/40111) as evidenced by Lee et al.(Journal of Orthopaedic Research).

With respect to claim 29, the reference of Lee et al.('111) discloses a method for producing functional cartilaginous tissue from a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate, wherein the method includes inoculating chrondrocytes into a scaffold or biocompatible substrate, placing the cell-seeded scaffold or substrate into a bioreactor, applying a strain-controlled deformational loading to the seeded scaffold or substrate via loading platens according to a load regime optimized for

cartilaginous tissue growth; and culturing the scaffold or substrate for a time sufficient to produce functional cartilaginous tissue (See page 14, lines 9-27; Example 6 and Example 10). Note, the reference of Lee et al.(Journal of Orthopaedic Research) is cited as evidence that the bioreactor employed in Example 10 includes loading platens and control electronics for providing the strain-controlled deformational loading of the scaffolds or substrates (See Figure 1 and pages 182-183 of Lee et al.(Journal of Orthopaedic Research)). The use of multiple references in a 35 USC 102 rejection is proper when the extra reference provides evidence of what already exists in the primary reference (See M.P.E.P. 2131.01).

With respect to claims 1, 30 and 61, the bioreactor employed by Lee et al.('111) includes a growth chamber and means for applying strain-controlled deformational loading via loading platens and means for controlling the loading platens that is capable of producing functional cartilage (See Figure 1 and pages 182-183 of Lee et al.(Journal of Orthopaedic Research)).

With respect to claims 2-5 and 22-28, in the absence of further positively recited structure of the device, the system of the primary reference is considered to be capable of producing and/or operating of tissue as recited in these dependent claims.

With respect to claims 13-19, the system of the primary reference is structurally capable of providing the loading regimes of claims 13-19.

With respect to claims 31-34, the reference of Lee et al.('111) discloses that the substrate material can be biodegradable, bioresorbable, biocompatible and/or non-resorbable (See page 8, lines 8-13).

With respect to claim 35, the implant material resulting from the treatment disclosed by the reference of Lee et al. ('111) is considered to produce an implant material with the claimed properties of claim 35.

With respect to claims 58-60, the bioreactor and/or platens are capable of producing tissue of a desired shape that can be implanted.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 45-51 and 54-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(WO 98/40111) as evidenced by Lee et al.(Journal of Orthopaedic Research).

The reference of Lee et al.('111) as evidenced by the reference of Lee et al.(J. Orth. Res.) has been discussed above.

With respect to the strain loading of claims 45-51, the reference of Lee et al.('111) (See page 14, line 9, to page 15, line 20) discloses that the object of the treatment system is to expose the tissue constructs to loading that resembles the physiological conditions typically encountered by the tissue being replace and/or repaired.

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the typical conditions that the desired tissue would be exposed to and operate the device to mimic those physiological conditions in terms of loading, frequency and length of time.

With respect to claims 54-57, while the reference of Lee et al.('111) discloses that the implant is used for repair of damaged connective tissue, the reference is silent with respect to the specifics of the implant (See page 16, lines 4-20). However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the specific type of cartilage produced based merely on the intend use of the cartilage in terms of the location in the body it is intended to be implanted.

11. Claims 6-12, 20, 21, 36-44, 52, 53, 62-64, 69, 71, 73, 74-76, 78, 80 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(WO 98/40111) as evidenced by Lee et al.(Journal of Orthopaedic Research) taken further in view of Nevo et al.(US 2002/0009805).

The reference of Lee et al.('111) as evidenced by the reference of Lee et al.(J. Orth. Res.) has been discussed above.

With respect to claims 6-12, 20, 21, 36-44, 52, 53, 62-64, 69, 71, 73, 74-76, 78, 80 and 82, while the reference of Lee et al. ('111) discloses that hydrostatic pressure is a known means for loading tissue implants prior to implantation (See page 14, lines 22-24), the instant claims require the combination of the strain and hydrostatic loading.

The reference of Nevo et al. discloses that it is known in the art to maintain tissue constructs under culture conditions that control the hydrostatic pressure that the tissue is exposed to (See paragraphs [0049] and [0059].

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the system of the primary reference to in include hydrostatic loading as suggested by Nevo et al. for the known and expected result of providing an additional means recognized in the art for ensuring that the cultured cells are exposed to conditions that mimic physiological conditions and for improving the contact of the culture medium within in pores of the porous scaffold material during the culture process. With respect to the specific loading conditions, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the typical conditions that the desired tissue would

be exposed to and operate the device to mimic those physiological conditions in terms of loading, frequency and length of time.

12. Claims 1-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al.(WO 98/40111) as evidenced by Lee et al.(Journal of Orthopaedic Research) in view of Carver et al.(Biotech. and Bioeng., Vol. 62).

The reference of Lee et al.('111) as evidenced by the reference of Lee et al.(J. Orth. Res.) has been discussed above.

If it is determined that the loading regime of the instant claims is different for that of the reference of Lee et al. and/or produces a tissue that is different from that of the reference of Lee et al., the following rejection is applicable.

With respect to independent claims 1, 29 and 61, while the reference of Lee et al. encompasses a loading regime for producing cartilaginous tissue, the loading regime is performed for only 48 hrs. and is considered a "short term" culture period while the instant claims could be considered to cover a "long term" culture period.

The reference of Carver et al. discloses that it is known in the art that "long term" cultures of cartilaginous tissue exposed to dynamic mechanical force results in tissue that is closer to natural tissue than the tissue resulting from "short term" culture (See page 166, second column, last paragraph, to page 167, first column, first paragraph; and the "Results" and "Discussion" sections).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to modify the system and method of the reference of Lee et al. so as to perform a "long term"

culture (up to 5 weeks) for the known and expected result of exposing the tissue of Lee et al. to long term dynamic mechanical loading as suggested by the reference of Carver et al. and thus producing a "functional" cartilage tissue.

With respect to claims 2-5 and 22-28, in the absence of further positively recited structure of the device, the system of the primary reference is considered to be capable of producing and/or operating of tissue as recited in these dependent claims.

With respect to claims 13-19, the system of the primary reference is structurally capable of providing the loading regimes of claims 13-19.

With respect to claims 31-34, the reference of Lee et al.('111) discloses that the substrate material can be biodegradable, bioresorbable, biocompatible and/or non-resorbable (See page 8, lines 8-13).

With respect to claim 35, the implant material resulting from the treatment disclosed by the reference of Lee et al. ('111) is considered to produce an implant material with the claimed properties of claim 35.

With respect to claims 58-60, the bioreactor and/or platens are capable of producing tissue of a desired shape that can be implanted.

With respect to the strain loading of claims 45-51, the reference of Lee et al.('111) (See page 14, line 9, to page 15, line 20) discloses that the object of the treatment system is to expose the tissue constructs to loading that resembles the physiological conditions typically encountered by the tissue being replace and/or repaired.

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the typical conditions that the desired tissue would

be exposed to and operate the device to mimic those physiological conditions in terms of loading, frequency and length of time.

With respect to claims 54-57, while the reference of Lee et al.('111) discloses that the implant is used for repair of damaged connective tissue, the reference is silent with respect to the specifics of the implant (See page 16, lines 4-20). However, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the specific type of cartilage produced based merely on the intend use of the cartilage in terms of the location in the body it is intended to be implanted.

With respect to claims 6-12, 20, 21, 36-44, 52, 53, 62-64, 69, 71, 73, 74-76, 78, 80 and 82, while the reference of Lee et al. ('111) discloses that hydrostatic pressure is a known means for loading tissue implants prior to implantation (See page 14, lines 22-24), the instant claims require the combination of the strain and hydrostatic loading.

The reference of Carver et al. discloses that it is known in the art to maintain tissue constructs under culture conditions that control the hydrostatic pressure that the tissue is exposed to (See "Compression/Perfusion System").

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the system of the primary reference to in include hydrostatic loading as suggested by Carver et al. for the known and expected result of providing an additional means recognized in the art for ensuring that the cultured cells are exposed to conditions that mimic physiological conditions and for improving the contact of the culture medium within in pores of the porous scaffold material during the culture process. With respect

to the specific loading conditions, it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine the typical conditions that the desired tissue would be exposed to and operate the device to mimic those physiological conditions in terms of loading, frequency and length of time.

Response to Amendment

13. The declaration under 37 CFR 1.132 filed 3/9/2006 is insufficient to overcome the rejection of claims 1-63 based upon Lee et al. and Lee and Bader as set forth in the last Office action because:

The declaration is not found to be persuasive because the product of Lee et al. has been compared to native tissue rather than the product produced by the loading regime of the instant claims. That is, the declaration does not provide any quantifiable evidence from which one of skill in the art could conclude that the final tissue product produced by the loading regime of the instant claims is different from the tissue produced by the loading regime of the device and method disclosed by the reference of Lee et al. as evidenced by the reference of Lee and Bader.

Response to Arguments

14. With respect to the rejection of claims 1-63 under 35 U.S.C. 102(b) and 103(a) as being unpatentable over Lee et al.(WO 98/40111) as evidenced by Lee et al.(Journal of Orthopaedic Research), Applicants argue that the rejection is improper for the following reasons.

Applicants argue (See pages 18-19 of the response filed 3/9/2006) that the reference of Lee et al. as evidenced by Lee and Bader does not produce a functional cartilaginous tissue.

Applicants point to the declaration filed under 37 CFR 1.132 to support this position. Applicants stress that the reference of Lee et al. does not provide any quantifiable evidence that the tissue produced by Lee et al. is a functional cartilaginous tissue. As a result, Applicants conclude that since Lee et al. does not produce a functional cartilaginous tissue, the reference cannot teach or suggest the claimed loading regime for producing such tissue and/or means for controlling.

In response, Applicants' comments are not found to be persuasive because the declaration does not compare the product produced by the claimed loading regime with the product of the reference of Lee et al. As a result, the Examiner is of the position that the device and method disclosed by the reference of Lee et al. as evidenced by the Lee and Bader meets the claim limitations of the instant claims in the absence of further positively recited claim language defining the claimed loading regime over that of the reference of Lee et al.

Applicants argue (See pages 18-19 of the response filed 3/9/2006) that the reference of Nevo does not remedy the deficiencies of the references of Lee et al. and Lee and Bader.

In response, the reference of Nevo was merely recite as a secondary teaching that suggested the use of hydrostatic pressure when culturing cartilage tissue.

Applicants also argue (See pages 20-21 of the response filed 3/9/2006) that the Examiner has improperly combined the references of Lee et al. and Lee and Bader when rejecting the claims under 35 USC 102. Applicants stress that one of ordinary skill in the art would not inherently known from Lee et al. that the bioreactor in Lee et al. contained loading platens and electronics.

In response, the Examiner disagrees. Example 10 of Lee et al. specifically recites that the device "as described in example 6 (Lee, D. A., and Bader, D. L., *Journal of Orthopaedic*

Research **15** (2) 181-188 (1997)" is used. Clearly one of ordinary skill in the art would recognize that the device of Lee and Bader, example 6, is being used in Example 10 of the reference of Lee et al.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys J. Corcoran can be reached on 571-272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

William H. Beisner
Primary Examiner
Art Unit 1744

WHB